

Uncertainty and COVID-19: how are we to respond?

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Introduction: why uncertainty matters

As if writing prophetically about the global COVID-19 pandemic, in 1984 Eddy suggested, 'Uncertainty creeps into medical practice through every pore. Whether a physician is defining a disease, making a diagnosis, selecting a procedure, observing outcomes, assessing probabilities, assigning preferences, or putting it all together, he (or she) is walking on very slippery terrain'.¹ COVID-19 has rapidly become a disease associated with unbridled uncertainty with its aetiology and management, for the healthcare systems and health professionals who provide care, and among its ultimate victims, patients and their families.

Frustratingly, uncertainty is not a simple or easily defined concept and situations of uncertainty often result from several inter-related factors. It has been characterised as an inadequate understanding, a sense of incomplete, ambiguous or unreliable information, and conflicting alternatives.² In the current COVID-19 pandemic, any given situation of uncertainty may be made up of several of these factors, but equally, there are many forms of uncertainty.³ Irrespective of its origin, we know uncertainty matters because when suppressed and ignored, consciously and subconsciously, it has potential to negatively impact on patients, their family, at a profoundly emotional level.⁴ It also affects health professionals and it has been argued their tolerance of uncertainty can affect levels of investigation, patient safety, as well as healthcare resource use.⁵ The authors of this commentary – an ITU physician, a palliative care physician and two social scientists – critically synthesise evidence from this grey area of uncertainty associated with COVID-19 and argue it is inescapable. In the face of the global proliferation of this disease and sense of urgency, they unite to consider how, in an area that is neither black nor white,

practical solutions that can be harnessed now, not to 'outsmart' uncertainty, but to acknowledge its presence and, where possible, to work more effectively and efficiently alongside it to improve patient and family care at a critical moment in their lives (Tables 1 and 2).

COVID-19: known unknowns and unknown unknowns

At the time of writing, there are over 3.6 million confirmed cases of COVID-19 across 187 countries/world regions, of whom more than 250,000 have now died.⁶ Despite these figures, our understanding of the disease is still very much in its infancy. Confusion is present about the uncertain denominator making true mortality figures hard to quantify compounded by the unknown prevalence of asymptomatic infection. Moreover, in many countries accurate testing equipment is inadequate.

We currently lack a sophisticated understanding of the COVID-19 disease process and particularly why some individuals and groups are more affected than others. Those severely affected by the disease are typically over-represented by those who are elderly, those with multiple morbidities and are frail, and mysteriously those from certain ethnic groups. However, the uncertainty of COVID-19 has resulted in catastrophic consequences, regardless of these contributory factors.

As yet, there are no effective therapies for COVID-19 and those available are essentially supportive or palliative. Treatments currently being tested include antimalarial, antiviral, immunomodulator and steroid drugs, often adaptive in design with multiple intervention arms, reducing the chance of patients being randomised to just placebo. However, the trade-off is potential harms may be present associated with multiple-drug interactions. For example, the

Table 1. Recommendations to address disease and health system uncertainties.

Disease uncertainties	
1.	Develop and evolve guidance: Guidelines that can be modified for local use to inform important areas of clinical practice. These will be largely based on expert opinion initially but should be strengthened as evidence evolves.
2.	Count: Strategies to achieve a true denominator that more accurately reflects the extent of COVID-19 and allows more effective public health strategies to be deployed.
3.	Be promiscuous with lessons learned: Shared learning for health professionals via webinars and remote conference calls among a host of 'experts' or specialty leaders to inform best practice.
4.	Build databases that can inform clinical care: Building knowledge from observational data by formulating datasets and databases to guide clinical practice with an awareness of limitations in data collected.
5.	Robust clinical trials: Future effective therapies need to be urgently tested as part of clinical research trials. Areas currently under investigation: antivirals, steroids, immunomodulators, antimalarials, anticoagulation techniques and convalescent plasma transfusion.
Health system uncertainties	
1.	<p>The four 'S': Four key domains are relevant to alleviate health system uncertainties associated with COVID-19:</p> <ul style="list-style-type: none"> • Stuff: adequate supplies of equipment and medication, e.g. opioids, anti-psychotics for delirium/nausea, antimuscarinic agents for secretions and syringe drivers, subcutaneous butterflies for medication management; • Staff: health professionals with relevant expertise, confidence and competence; preparation of protocols and guidelines that can be adapted locally for practice, presence of grief/bereavement counselors; • Space: maximising and upgrading existing wards and beds/facilities to accommodate sicker patients and identifying non-clinical areas to be repurposed and transitioned promptly to respond to further COVID-19 'peaks'. • Systems: care plans in place for all patients that are shared electronically and seamlessly across care settings, including paramedics; liaison across provider networks to access knowledge for clinicians needing consultation support.²³
2.	Prepare new systems more specific to pandemics: These may include reconfiguration of hospital sites and services into 'clean' and 'dirty' sites, protecting patients and staff, allowing easier delineation between COVID-19 and non-COVID-19 related diseases; formation of triage and 'reverse triage' pathways based for those most likely to benefit in the event demand for medical services significantly outweigh supply, while ensuring fair access for everyone where possible.
3.	Learn from uncertainty: Uncertainty is a starting point for quality improvement. Uncertainty may expose preventable variation, erratic practices, safety errors or near misses, or areas in which new knowledge/new processes are valuable.

American College of Cardiology has issued a warning statement of the potential harm and higher risk of mortality when combining hydroxychloroquine with azithromycin.⁷

Vagueness extends to an incomplete understanding of patient outcomes. Until recently, mortality figures typically included only hospital deaths but not community deaths, including care homes, confusing the true incidence of the disease. For those with severe enough symptoms to be admitted to hospital, their routes tend to take one of two roads, both of which may lead to a chasm. Those with the best prospects of survival may end up in the intensive care unit whereas those with more underlying problems may be sent to an acute medical unit where they may succumb or

survive. Specifically, outcomes data for intensive care unit patients is biased towards those with shorter length of stay because they are still receiving care at the time of analysis, an unavoidable occurrence during a constantly changing pandemic.⁸ At present, no information is available on longer-term survival or non-mortality-related outcomes, including quality of life influenced by physical disability, psychosocial morbidity and new dependency needs.⁹

In turbulent COVID-19 waters, health systems are ships that require navigation

The COVID-19 pandemic is presenting unprecedented uncertainty in terms of how healthcare

Table 2. Recommendations to address health professional, patient and family uncertainty.

Health professional uncertainties	
1.	Admit uncertainty is not a failing: It has been suggested that appropriate expressions of uncertainty can lead to stronger healthcare professional–patient/family relationships, creating trust instead of unnecessary anxiety.
2.	All health professionals have an Achilles heel: Burnout, moral distress and moral injury have been identified as a significant issue among ICU and other health professionals. Supportive systems must be devised to caring for those working in ICU and other hospital settings, even before difficulty is evident.
3.	Rehearse situations of uncertainty individually and collectively: Identifying a priori issues health professionals anticipate as being uncertain. Reflections from clinical practice of situations that make health professionals feel uncomfortable, e.g. type of patient, challenging diagnosis, system-related dilemma – what worked and why and what did not. Rather than being caught unaware, this appraisal offer preparation for future situations of uncertainty.
4.	Be aware of cognitive biases: Yearning for situations of certainty amplifies the likelihood of cognitive biases that compromise logical reasoning. Pause and consider the situation and, better still, discuss with colleagues.
5.	Uncertainty should be taught to health professionals: Health professionals must challenge the cultural and educational systems set up to reward certainty, and promote a shift in perception of uncertainty as being negative. Medical and nursing are now incorporating more ‘real-life’ clinical learning, case-based approaches and training in health systems.
Patient and family-centred uncertainties	
1.	Patients/families as allies: Poor communication has previously been a major failing for those dying in hospital. Talking openly, yet sensitively, with patients with COVID-19 and their families about their situation, rehearsing their goals of care if their situation worsens. Consider what they would be willing to ‘trade-off’ to live longer confers clearer information for both patients and health professionals to plan.
2.	Help is available with difficult conversations: The ‘Serious Illness Conversations Guide’ www.ariadnelabs.org and ‘VitalTalk’, a US-developed ‘open source’ primer: https://tinyurl.com/ybvqqfjt offer excellent prompts for challenging discussions.
3.	Be imaginative: Since most families cannot be physically present as a consequence of visiting restrictions, ICU nurses are quickly finding creative ways to communicate with the families of patients with COVID-19, for example, video-conferencing for example https://tinyurl.com/ybvgr5le .
4.	Getting ‘into the shoes’ of the patient/family: The greatest security for a highly anxious patient (and their family) will be hearing that regardless of the situation of uncertainty health professionals will not abandon them. This involves empathy or (i) ‘seeing the world as the patient sees it’; (ii) ‘understanding the patient’s current feelings’; (iii) ‘being non-judgmental’; and (iv) ‘communicating that one understands’.

ICU: intensive care unit.

systems should respond¹⁰ and exists at the level of structures and processes of care. Specifically, structural uncertainty relates to physical environments of care, medical equipment and consumables. Services are trying to extrapolate from emerging and incomplete data to guide levels of resources required by patients, confused by additional uncertainty as to whether subsequent peaks in COVID-19 may be expected. Hospital beds, intensive care units and their associated equipment, including ventilators and infusion pumps, are vital for the treatment of patients with a severe illness. However, previously untested models have been developed to identify that need.

At the most mundane level uncertainty includes basic hospital resources, medication and the highly publicised provision of personal protective equipment. Not knowing also extends to the location of care. For example, there is evidence that while the number of hospitals beds devoted to COVID-19 has been reducing, there have been unpredicted increases in the level of care provided by nursing homes to frail, elderly people with complex needs, against a backdrop of limited staff and resources.

Moving from structures to processes of care, there is considerable uncertainty concerning how to effectively process and manage patients who have tested

positive for COVID-19 and those who have not, particularly if they present in emergency departments, a concern as the COVID-19 nasopharyngeal swab has a relatively high false-negative rate.¹¹ If patients are falsely screened-negative they may be sent to a 'clean ward' environment where they are potentially subjecting other patients and health professionals to risk. Conversely, if based on symptoms they are assumed positive and then located onto a 'dirty ward' but subsequently turn out negative, then these patients are in turn put at risk, particularly if they are already vulnerable.

The peak of this pandemic may stretch systems and the decisions required to identify which COVID-19 patients are most likely to benefit from escalating care (including admission to the intensive care unit). These judgements are beset with health process-related uncertainties. It is here that questions should be asked whether decision support aids in line with the best available evidence. The COVID-19: Rapid Guidance for Critical Care developed by NICE emphasises choices be based on the 'likelihood that a person will recover ... to an outcome that is acceptable to them'.¹² However, from what we do know, considerable prognostic uncertainty is present.¹³ Where possible, clinicians should attempt to ascertain patients' wishes and values regarding the escalation of care, particularly those who exhibit signs of impending or established organ failure. This should be factored into whether or not an escalation of care to an intensive care unit is appropriate, is in their best interests and acceptable to them.¹⁴ However, in a pandemic scenario, it may be practically difficult to engage in lengthy conversations with acutely unwell patients. In addition, under pandemic conditions, where the availability of resources remains in doubt, it may be much harder to argue 'all patients be treated without discrimination because everyone is of equal value'¹⁵ with emphasis on their autonomy. Here, the concept of utilitarianism governing how health systems operate under stress may override this. Decisions to admit might also be influenced by health professionals' implicit cognitive biases¹⁶ to compensate for health system uncertainties regarding intensive care unit bed availability.

People at the epicentre of uncertainty: health professionals, patients and their families

In the face of uncertainty, health professionals may react variably where their training has deliberately focused them towards specialism. However, the trade-off is that there is less personal adaptability

for cross-specialty cover and confidence required in the current pandemic. As more health professionals deliver care outside their comfort zones, this has the potential for over-investigation, overtreatment, or its opposite, that may compromise patient safety.⁵

Health professionals who believe they are uncertain about how a patient's condition may progress or respond to treatment might feel they have let patients and families down. Moreover, some might make clinical decisions they feel uncomfortable about or disagree with. As a consequence, they may become candidates for 'moral injury' resulting in stress, depression and post-traumatic stress disorder.¹⁷ Many patients cared for with COVID-19 may be 'ill enough to die'. In hospital settings and the absence of family members, health professionals may well be required to comfort these individuals but feel that they lack confidence and competence to do so to good effect, particularly when they are not normally exposed to 'life and death' situations in their usual practice. Doubt also extends beyond the patients health professionals care for. For example, they might be working in new ward environments where the stability and familiarity of a known clinical team are not present.

Pre-pandemic times, the existence of an information mountain might have provided a myth of certainty for the wider public. Paradoxically, given the current COVID-19 climate where we are exposed to an 'infodemic' of news from multiple sources with multiple, contradictory messages, certainty is now an illusion and anxiety is omnipresent. For those individuals with COVID-19 sick enough to be admitted to hospital, they may rapidly become isolated from families, especially where visiting restrictions are in force. Both parties may be anxious about this period of profound separation and when, or even if, they will be reunited, survive and, if so, what it might look like. This echoes closely with Florence Nightingale's concern for those in vulnerable positions, 'Apprehension, uncertainty, waiting, expectation, fear of surprise, do a patient more harm than any exertion. Remember he is face to face with his enemy all the time' (p53).¹⁸ We know from qualitative studies of illnesses pre-dating COVID-19 uncertainty can negatively impact on patients' experiences and outcomes of care. Where uncertainty about their situation is present, patients become preoccupied to such an extent that their sense of self is changed.¹⁹ Patients and their families often want to discuss their situation of uncertainty; however, this rarely happens.²⁰

Patients may experience an environment of care alien to any previous hospital experience which may be profoundly disconcerting. The requirement of

health professionals to wear personal protective equipment and the possible absence of continuity of health professionals caring for them has potential to amplify this and more so if they are already confused as a direct consequence of their illness or from other co-morbidities.¹⁶

Before the COVID-19 pandemic, evidence suggests exploring patients' wishes regarding admission to the intensive care unit were uncommon. This is despite evidence of older patients' decreased willingness to want burdensome therapy or to risk severe disability to avoid death.²¹ Patients therefore may need assistance to recognise possible 'trade-offs' among their values and to understand the relationship between what is important to them and their families and treatment preferences.²²

If they are not able to obtain timely and accessible information and updates about loved ones, families might be in a state of heightened anxiety. Evidence from an evaluation of a UK-developed intervention to serve patients whose situations were clinically uncertain and where there was a risk they may die during their hospital stay observed inconsistencies in information family members received with concomitant repercussions for satisfaction.²⁰ Additionally, families may challenge healthcare decisions if they do not understand what is happening.

Multiple barriers to a discussion of prognosis with patients with COVID-19 and their families may be present including lack of time, lack of expertise and a fear of taking away hope. It is also possible health professionals may have overriding concerns not to share their uncertainty about a patient's situation, believing patients and their families might question their competency or honesty, resulting in loss of professional confidence. Nevertheless, it has been shown appropriate expressions of uncertainty do indeed lead to stronger health professional-patient family relationships.

Conclusions

In the current global pandemic of COVID-19, we can not eliminate uncertainty or the multitude of questions and doubts it creates. We argue a paradigm focused purely on its removal is futile. However, it can be managed far better than is done now to minimise its damage. The main business in hand must be for health professionals to support those patients and their families that occupy the 'grey Covid-19 zone' and build trusting empathetic relationships with them where uncertainty can be communicated in such a way that enables shared decision-making to reduce distress.⁵ We must then learn from this pandemic and develop strategies to change professional

cultures that have thrived on developing antibodies to uncertainty and avoiding its presence.

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References

1. Eddy DM. Variations in physician practice: the role of uncertainty. *Health Aff (Millwood)* 1984; 3: 74–89.
2. Lipshitz R and Strauss O. Coping with uncertainty: A naturalistic decision-making analysis. *Organ Behav Hum Decis Process* 1997; 69: 149–163.
3. Kirkegaard P, Risor MB, Edwards A, Junge AG and Thomsen JL. Speaking of risk, managing uncertainty: decision-making about cholesterol-reducing treatment in general practice. *Qual Prim Care* 2012; 20: 245–252.
4. Schwarze ML and Taylor LJ. Managing Uncertainty — Harnessing the Power of Scenario Planning. *N Engl J Med* 2017; 377: 206–208.
5. Simpkin AL and Schwartzstein RM. Tolerating Uncertainty — The Next Medical Revolution? *N Engl J Med* 2016; 375: 1713–1715.
6. Johns Hopkins University & Medicine. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins USA: Johns Hopkins University & Medicine, Coronavirus Resource Centre, 2020.
7. Simpson TF, Kovacs RJ and Stecker EC. Ventricular arrhythmia risk due to hydroxychloroquine-azithromycin treatment for COVID-19. *Cardiology Magazine*. USA: American College of Cardiology, 2020.
8. ICNARC. ICNARC report on COVID-19 in critical care. London, UK: Intensive Care National Audit & Research Centre (ICNARC), 2020, p. 17.
9. Kress JP and Hall JB. ICU-acquired weakness and recovery from critical illness. *N Engl J Med* 2014; 370: 1626–1635.
10. Abbasi K. COVID-19: fail to prepare, prepare to fail. *J R Soc Med* 2020; 113: 131.
11. Yang Y, Yang M, Shen C, et al. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. *medRxiv* 2020: 2020.02.11.20021493.
12. NICE. *COVID 19: Rapid Guidance for Critical Care*. London: National Institute for Health and Care Excellence, 2020.

13. Wynants L, Van Calster B, Bonten MMJ, et al. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. *BMJ* 2020; 369: m1328.
14. Swiss Academy of Medical Sciences. COVID-19 pandemic: triage for intensive-care treatment under resource scarcity. *Swiss Medical Weekly* 2020; 150: w20229.
15. Intensive Care Society. Clinical Guidance: Assessing whether COVID-19 patients will benefit from critical care, and an objective approach to capacity challenges. London: Intensive Care Society 2020.
16. Koffman J, Yorganci E, Yi D, et al. Managing uncertain recovery for patients nearing the end of life in hospital: a mixed-methods feasibility cluster randomised controlled trial of the AMBER care bundle. *Trials* 2019; 20: 506.
17. Cook D and Rocker G. Dying with Dignity in the Intensive Care Unit. *N Engl J Med* 2014; 370: 2506–2514.
18. Nightingale F. *Notes on Nursing: What it is and What it is Not (1860)*. Appleton-Century: Digireads.com, 2010.
19. Etkind SN, Bristowe K, Bailey K, Selman LE and Murtagh FE. How does uncertainty shape patient experience in advanced illness? A secondary analysis of qualitative data. *Palliat Med* 2017; 31: 171–180.
20. Bristowe K, Carey I, Hopper A, et al. Patient and carer experiences of clinical uncertainty and deterioration, in the face of limited reversibility: A comparative observational study of the AMBER care bundle. *Palliat Med* 2015; 29: 797–807.
21. Philippart F, Vesin A, Bruel C, et al. The ETHICA study (part I): elderly's thoughts about intensive care unit admission for life-sustaining treatments. *Intensive Care Med* 2013; 39: 1565–1573.
22. Bernacki R, Hutchings M, Vick J, et al. Development of the Serious Illness Care Program: a randomised controlled trial of a palliative care communication intervention. *BMJ Open* 2015; 5: e009032.
23. Downar J and Seccareccia D. Palliating a pandemic: 'all patients must be cared for'. *J Pain Symptom Manage* 2010; 39: 291–295.